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Correlations of Placental Vascular Anatomy and Clinical Outcomes in 69 Monochorionic Twin Pregnancies

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Monochorionic monozygotic twins frequently suffer complications from the presence of vascular anastomoses in their monochorionic placentas. Also, sharing of perfusion zones may be unequal, leading to marked growth discordance.

This paper analyzes four measures of perinatal outcome (gestational age at delivery, perinatal mortality, birth weight discordance, and presence/absence of hydramnios) according to the vascular patterns of the monochorionic placentas. The worst clinical outcomes were associated with arterio-venous anastomoses in the absence of arterio-arterial and veno-venous anastomoses.

The vascular patterns of monochorionic placentas cause significant fetal environmental differences within pairs of monochorionic monozygotic twins. These differences may cause life-long discordance for several phenotypic traits that are not genetically based, and which cause monochorionic monozygotic twins to be "non-identical."

KEY WORDS: **disease in twins, monozygotic twins, growth discordance in twins**

INTRODUCTION

It has been a basic tenet of twin research that newborn monozygotic twin pairs are "identical" tabulae rasae on which are subsequently inscribed environmental events that may cause phenotypic discordance. Accompanying papers show the extent to which post-zygotic events cause some monozygotic pairs to be genotypically dissimilar [Machin, 1996; Bamforth et al., 1996; Goodship et al., 1996]. Recently, Machin et al. [1995] showed that dichorionic monozygotic twin pairs have superior prenatal and perinatal outcomes in comparison with monochorionic twin pairs, the latter sharing truly single placentas.

This paper analyzes the prenatal placental environmental difference between monozygotic monochorionic twin pairs that cause high rates of adverse outcomes. The timing of events leading to dichorionic and monochorionic monozygotic twinning are relatively early (less than 2 days post-conception) and late (2–14 days post-conception), respectively, and these differences may also influence early embryogenesis in different ways. However, the structure and function of the monochorionic placenta is a major factor in embryonic and fetal development, since it can impose discordant prenatal environmental influences within monochorionic twin pairs. Indeed, the risks of major complications and perinatal death in twin pregnancies (significantly higher than in singletons) [Kovacs et al., 1989; Spellacy et al., 1990; Kleinman et al., 1991] are higher among monochorionic twins, who constitute about two-thirds of monozygotic twins and 20% of all twins. Complications in monochorionic twin pregnancies are largely attributable to the presence of vascular anastomoses in the single monochorionic placenta. Criteria for prenatal diagnosis of monochorionic status are well established [Cheung et al., 1990], but there are at present no non-invasive methods for pre-natal study of the pattern of vascular anastomoses.

In the presence of vascular anastomoses, various interactions can occur between the circulations of monochorionic twins; these are generally referred to as twin-twin transfusion and twin-reversed arterial perfusion. There are no generally agreed criteria for the prenatal diagnosis of twin-twin transfusion and twin-reversed arterial perfusion, which have variable clinical courses, both in timing and severity. Although growth discordance and hydramnios are common in twin-twin transfusion and twin-reversed arterial perfusion, they are also found for other reasons both in monochorionic and

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dichorionic twins. In particular, growth discordance is seen with equal frequency and severity in monochorionic and dichorionic twin pregnancies [Danskin and Nielson, 1989; Grennert et al., 1980]. Growth discordance in monochorionic twins depends largely on the unequal sharing of venous returns from the placenta, although this is modified by the the presence of vascular anastomoses [Bendon and Siddiqui, 1989].

Since many of the complications of monochorionic twin pregnancy are attributable to the vascular status of the monochorionic placentas, we decided to classify monochorionic twin pregnancies on the basis of the vascular patterns of the placentas as determined after delivery; the vascular patterns were then correlated with the clinical outcomes by gestational age at delivery, perinatal mortality rate, growth discordance, and hydramnios. In some cases a definite diagnosis of twin-twin transfusion was assigned.

Vascular patterns were found to fall into 15 groups, some of which were associated with high rates of complications and mortality. The anatomic patterns of vascular anastomoses were usually simple, and could readily have been treated with laser occlusion therapy when indicated [De Lia et al., 1993].

MATERIALS AND METHODS

All twin placentas were examined over a 4-year period at the University of Alberta Hospitals, which is a tertiary perinatal referral centre. During this time, 80 pairs of monochorionic twins were delivered, of whose placentas 69 were suitable for detailed analysis of vascular anastomoses. The remaining 11 placentas were either fragmented or formalin-fixed. After determination of monochorionic status by the presence of two layers of amnion and no chorion in the septum, vascular perfusion studies were carried out by catheterization of one or more umbilical vessels close to the insertion of the cords into the placenta. Perfusion studies were not done if inspection showed no areas of potential vascular anastomoses.

Vascular status was classified in two main ways. First, the types of vascular anastomoses were analyzed as arterio-arterial, veno-venous, arterio-venous, and combinations of these types. Second, the monochorionic parenchyma was assessed for equal/unequal sizes of venous fields returning blood to each twin cord (Fig. 1). Of all the possible patterns of venous sharing and vascular anastomoses, 15 were actually found in this series (Fig. 2).

Clinical outcomes were recorded from chart review; 4 types of outcomes were used: perinatal mortality rate, hydramnios, gestational age at delivery, and growth discordance.

All the monochorionic twins were confirmed as monozygotic by DNA restriction fragment length polymorphism analysis, using three endonuclease probes.

For the analysis of perinatal mortality rate and hydramnios by vascular anastomoses status, simple chi-square tests were used. For the analysis of gestational age at delivery and growth discordance, various non-parametric statistical methods were used.

RESULTS

During the period of study, the perinatal death rates in monochorionic and dichorionic twins were 16% and 4%, respectively.

The patterns of vascular anastomoses in the 69 monochorionic placentas are shown diagrammatically in Figure 2. The most common pattern (#13, Fig. 3) was arterio-arterial with unidirectional arterio-venous vascular anastomoses and unequal venous sharing; absence of vascular anastomoses with equal venous sharing (#1)

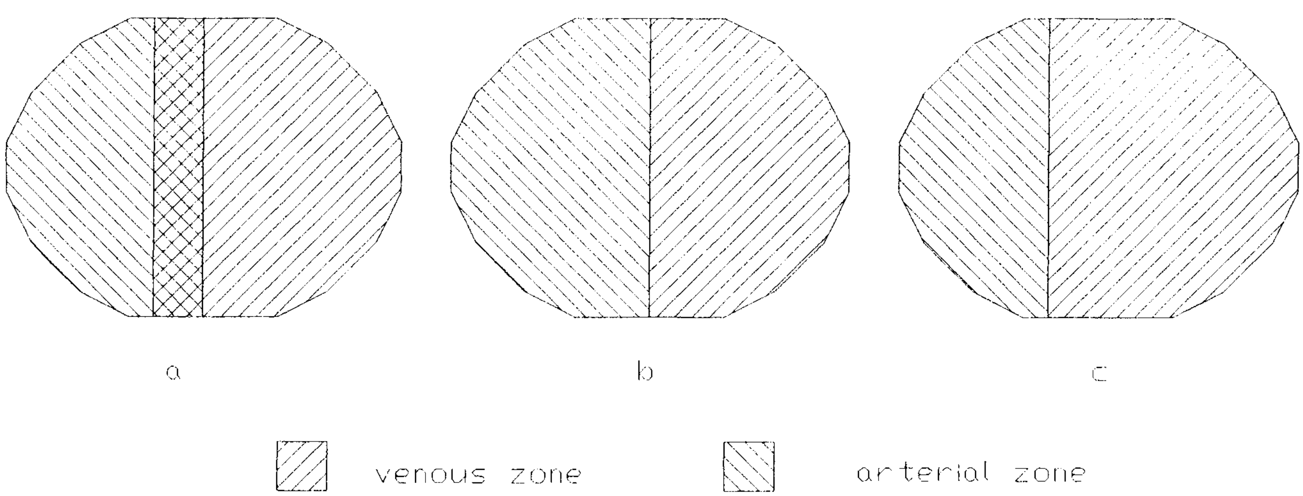

Fig. 1. Diagrammatic representation of effects of equal and unequal arterial and venous zone sharing. **a:** Arterial zone of twin on left is smaller than venous zone of twin on right. In the absence of superficial anastomosis, twin-twin transfusion will develop. **b:** Equal arterial and venous zones for each twin. Regardless of presence or absence of superficial anastomoses, these pregnancies are usually uncomplicated and go through to late third trimester. **c:** Arterial and venous zones of twin on the left are smaller than those of twin on the right. Twin A is likely to be growth-retarded, but there is no twin-twin transfusion.

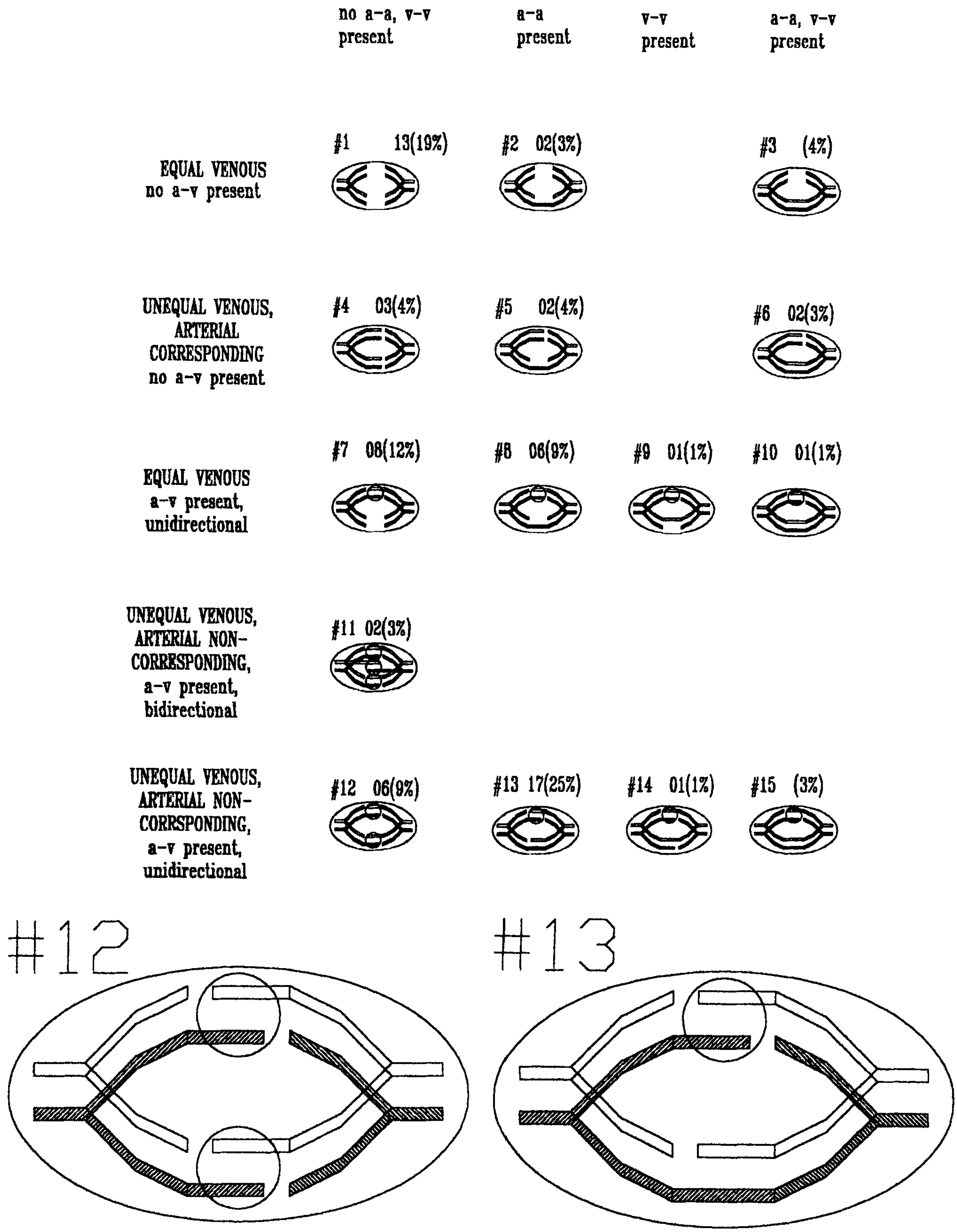

Fig. 2. The frequencies of the 15 types of vascular anastomoses and venous sharing. Arteries are shown in solid and veins are open. Rings indicate zones of arterio-venous anastomoses. **Inserts** show types 12 and 13 in detail. Type 13 was the most common while type 12 was associated with 83% perinatal mortality (Table I).

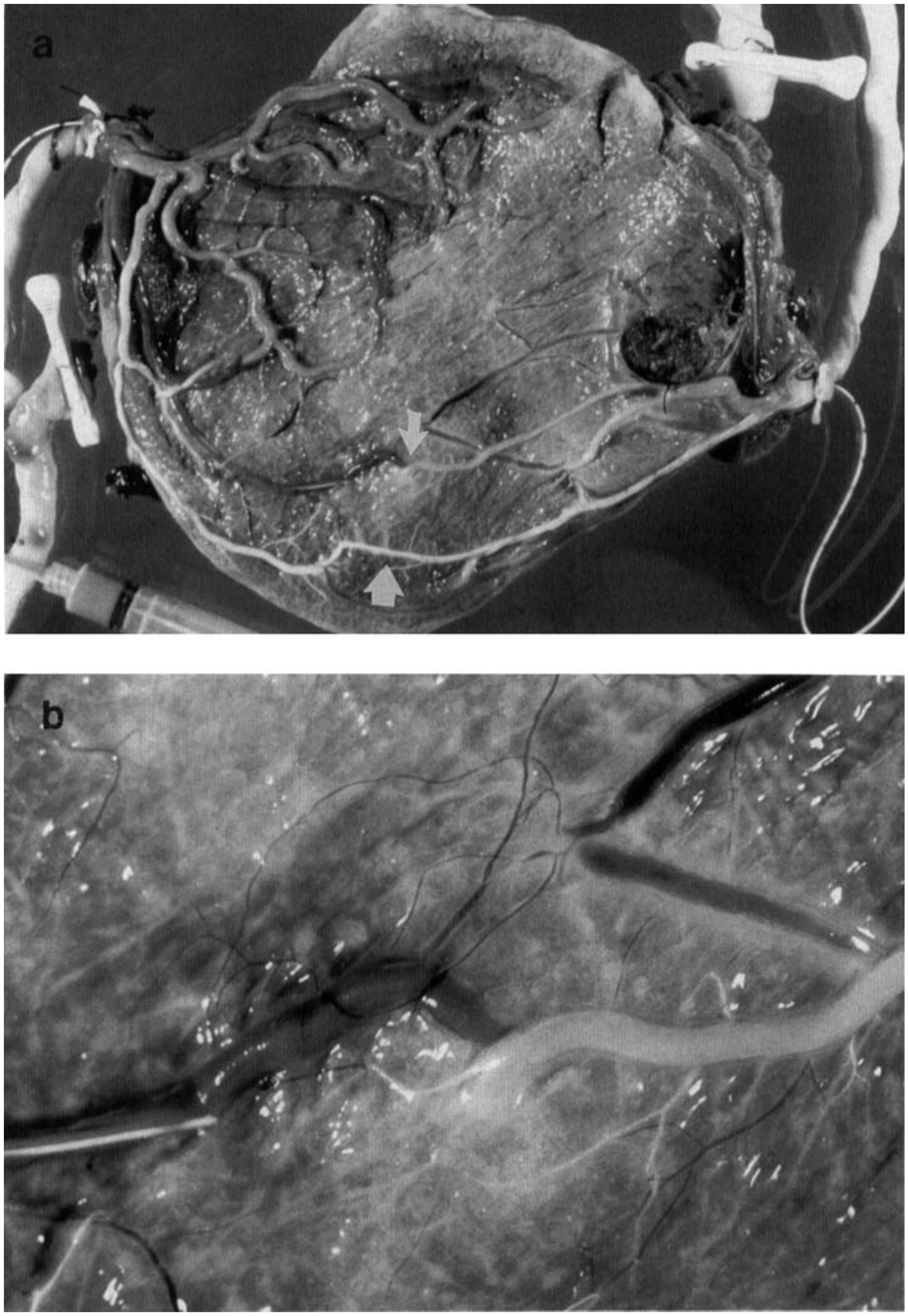

Fig. 3. Type 13 vascular anastomosis. The twins were markedly growth discordant, but there was no twin-twin transfusion. **a:** There is an arterio-arterial anastomosis (large arrow) and a zone of arterio-venous anastomosis (small arrow) caused by unequal venous sharing. **b:** Detail of the arterio-venous anastomosis, which is at villous level. The artery (right) and vein (left, with catheter tip) meet end-to-end but do not anastomose on the surface. There is unequal venous sharing.

was also common. The highest complication rate was seen in group #12 (Fig. 4), with absent superficial vascular anastomoses, arterio-venous vascular anastomoses and unequal venous sharing. These patterns are correlated with perinatal mortality, hydramnios, mean gestational age, and mean growth discordance in Table I.

1. Perinatal Mortality

There were 22 perinatal deaths (15.9%) among the 138 monochorionic twins. By chi-square test, there were significantly higher rates ($P < 0.05$) of perinatal mortality in some vascular anastomotic groups as follows:

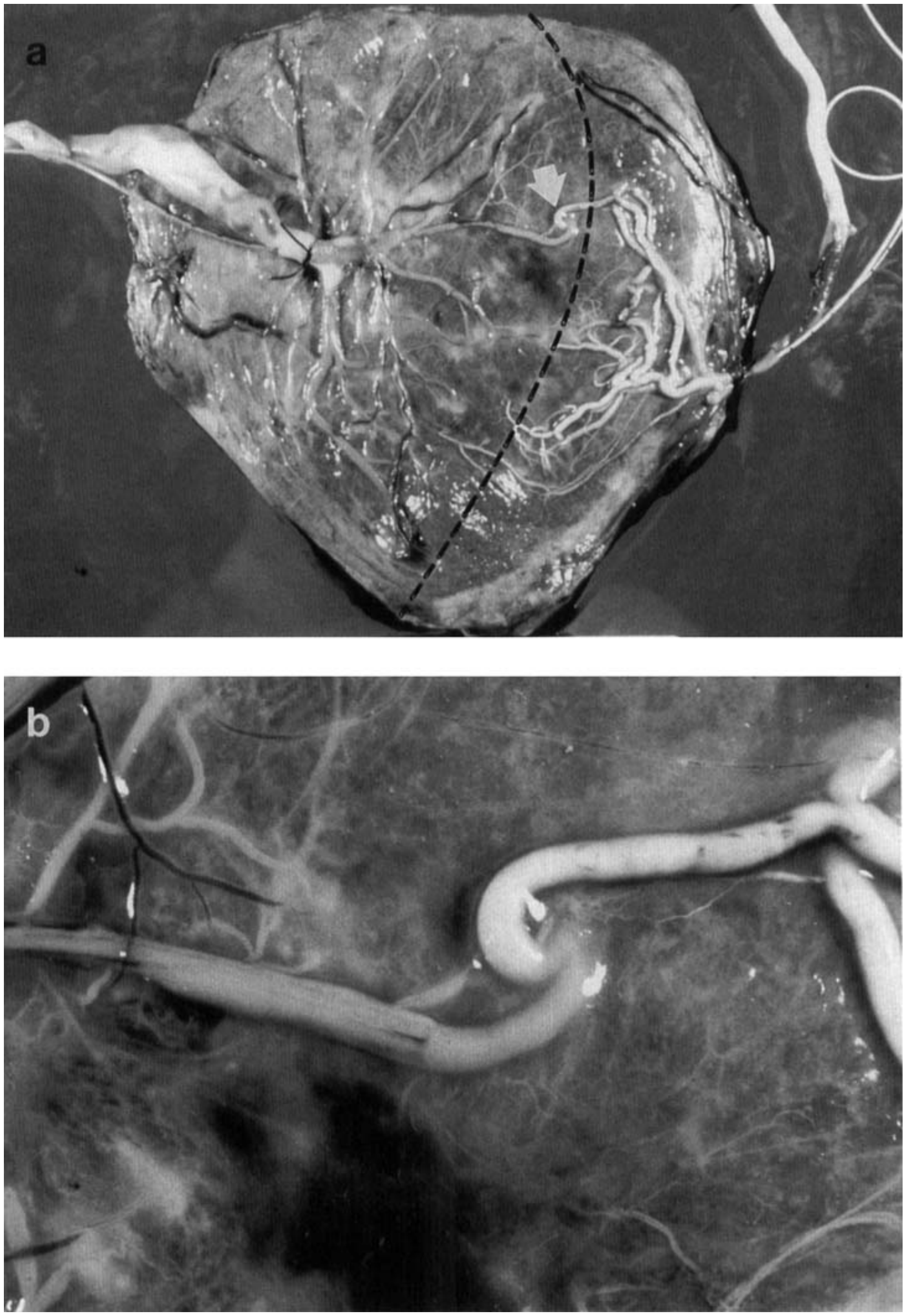

Fig. 4. Type 12 vascular anastomosis. The twins died of acute pre-natal twin-twin transfusion. **a:** The cord of the recipient (left) is edematous, while that of the donor is thin (right). The perfusion zone of the donor is smaller, originating from a marginally inserted cord. There are no superficial anastomoses, but an area of arterio-venous anastomosis is present (arrow). The dotted line marks the approximate equator between the two venous perfusion zones. **b:** Detail of the arterio-venous anastomosis. The artery of the donor (right) meets end-on with the vein of the recipient. The anastomoses are at villous level. It is this pattern of incompensated arterio-venous anastomosis that causes prenatal twin-twin transfusion.

Superficial vascular anastomoses absent Equal venous sharing (Groups 1, 7) Perinatal mortality 6/42 (14.3%)	**versus**	Superficial vascular anastomoses present Equal venous sharing (Groups 2, 3, 8–10) Perinatal mortality 0/26	Superficial vascular anastomoses absent Unequal venous sharing (Groups 4, 11, 12) Perinatal mortality 13/22 (27.2%)	Superficial vascular anastomoses present Unequal venous sharing (Groups 5, 6, 13–15) Perinatal mortality 3/48 (6.25%)

TABLE I. Perinatal Mortality, Incidence of Hydramnios, Mean Gestational Age, and Mean Growth Discordance Analyzed by the 15 Vascular Patterns, No. (%)

Group	Group total	Perinatal mortality	Hydramnios	Mean gestational age	Mean growth discordance
1	26	2 (8)	—	34.3	12.7
2	4	—	—	34.0	8.1
3	6	—	—	35.7	12.9
4	6	1 (17)	—	34.7	37.7
5	4	—	2 (50)	35.5	23.3
6	4	—	—	33.0	19.3
7	16	4 (25)	4 (25)	32.0	8.2
8	12	—	—	35.0	4.7
9	2	—	2 (100)	29.0	20.9
10	2	—	0	37.0	15.5
11	4	2 (50)	—	34.5	14.4
12	12	10 (83)	12 (100)	26.7	34.7
13	34	3 (9)	4 (12)	34.9	13.5
14	2	—	2 (100)	33.0	40.1
15	4	—	2 (50)	33.5	36.9
Total	138	22 (16)	28 (20)	33.6	16.1

Arterio-arterial vascular anastomoses absent Equal venous sharing (Groups 1, 7, 9) Perinatal mortality 22/52 (42.3%)	Arterio-arterial vascular anastomoses present Equal venous sharing (Groups 2, 3, 8–10) Perinatal mortality 0/16
Arterio-arterial vascular anastomoses absent Unequal venous sharing (Groups 4, 11, 12) Perinatal mortality 19/32 (59.3%)	Arterio-arterial vascular anastomoses present Unequal venous sharing (Groups 5, 6, 13, 15) Perinatal mortality 3/38 (7.9%)
All other groups (Groups 1, 3, 4, 6, 7, 9–12, 14, 15) Perinatal mortality 31/74 (40.5%)	Arterio-arterial vascular anastomoses only present (Groups 2, 5, 8, 13) Perinatal mortality 3/54 (5.6%)
Arterio-venous vascular anastomoses present (Groups 7–15) Perinatal mortality 19/88 (21.6%)	Arterio-venous vascular anastomoses absent (Groups 1–6) Perinatal mortality 3/50 (6.0%)
Superficial vascular anastomoses absent (Groups 1, 4, 7, 11, 12) Perinatal mortality 19/64 (29.7%)	Superficial vascular anastomoses present (Groups 2, 3, 5, 8–10, 13–15) Perinatal mortality 3/74 (4.1%)
Arterio-arterial vascular anastomoses absent (Groups 1, 4, 7, 9, 11, 12, 14) Perinatal mortality 19/34 (55.9%)	Arterio-arterial vascular anastomoses present (Groups 2, 3, 5, 6, 8, 10, 13, 15) Perinatal mortality 3/54 (5.6%)

2. Presence of Hydramnios

There were 14 cases (20.3%) of severe hydramnios among the 69 monochorionic twin pairs. By chi-square test, there were significantly higher rates ($P < 0.05$) of severe hydramnios in some vascular anastomoses groups as follows:

Vascular anastomoses present	**versus**	Vascular anastomoses absent
(Groups 2, 3, 5–15) Hydramnios present 14/53 (26.4%)		(Groups 1, 4) Hydramnios present 0/16
Vascular anastomoses present Unequal venous sharing (Groups 5, 6, 8–10, 13–15) Hydramnios present 11/32 (34.4%)		Vascular anastomoses absent Unequal venous sharing (Groups 4, 11, 12) Hydramnios present 0/3
Arterio-venous vascular anastomoses present (Groups 7–15) Hydramnios present 13/44 (29.6%)		Arterio-venous vascular anastomoses absent (Groups 1–6) Hydramnios present 1/25 (4%)
Superficial vascular anastomoses absent Unequal venous sharing (Groups 4, 11, 12) Hydramnios present 6/10 (60.0%)		Superficial vascular anastomoses present Unequal venous sharing (Groups 5, 6, 13–15) Hydramnios present 5/25 (20.0%)
All other groups Unequal venous sharing (Groups 4, 6, 11, 12, 14, 15) Hydramnios present 8/16 (50%)		Only arterio-arterial vascular anastomoses present Unequal venous sharing (Groups 5, 13) Hydramnios present 3/19 (15.8%)

3. Gestational Age at Delivery

There were large differences in the frequencies of preterm delivery between the monochorionic and dichorionic twins (Table II).

In the analysis of monochorionic twins, the non-parametric method of Kruskal-Wallis was used for single factor analysis of variance with tied ranks. There were no cases of delayed delivery of the second twin. The 15 individual vascular anastomoses groups were compared with each other, and the following pairs were highly significantly different:

Group 13 versus group 1, 7, 8, 12
Group 01 versus groups 7, 8, 12

TABLE II. Percentage of Dichorionic and Monochorionic Twins Born at Various Gestational Ages

	Gestational age at delivery (weeks)		
Chorionicity	<28	29–36	>37
Dichorionic	3	59	37
Monochorionic	15	58	27
All	8	59	33

Group 07 versus group 12
Group 08 versus group 12

In comparing larger, combined patterns of vascular anastomoses, Welch's t-test showed that the following groups were highly significantly different ($P < 0.05$):

Superficial vascular anastomoses present	**versus**	Superficial vascular anastomoses absent
Arterio-arterial vascular anastomoses present		Arterio-arterial vascular anastomoses absent

4. Growth Discordance

Growth discordance was expressed as the difference in birth weights of pairs as a percentage of the birth weight of the heavier twin. Stillborn cases were excluded.

Frequency and severity of growth discordance were equal in monochorionic and dichorionic twins (Table III).

A single factor analysis of variance (Model II Anova) was done, and a Tukey test was used to compare mean birth weight discordance in the 5 largest vascular anastomoses groups, i.e., groups 1, 7, 8, 12, 13. The following pairs were highly significantly different:

Group 12 versus groups 1, 7, 8, 13

For comparison of the larger, combined groups, a two-tailed t-test was used. Highly significantly different birth weight discordances were found, as follows:

Superficial vascular anastomoses absent	**versus**	Superficial vascular anastomoses present
Equal venous sharing		Unequal venous sharing

DISCUSSION

From 5 published series, 83% of monochorionic placentas had vascular anastomoses; of these 70% had arterio-arterial vascular anastomoses, 48% had arterio-venous vascular anastomoses, and 23% had veno-venous vascular anastomoses [Benirschke, 1961; Strong and Corney, 1967; Galea et al., 1982; Arts and Lohman, 1971; Sekiya and Heifetz, 1977]. In one series, the highest perinatal mortality rate occurred in the presence of veno-venous only, and the higher frequency of twin-twin transfusion was found in the group with arterio-arterial and arterio-venous vascular anastomoses [Yoshida and Soma, 1984].

In this study, we took account of equality/inequality of venous sharing as well as the status of vascular anastomoses. We showed that an important confounding cause of growth discordance in the absence of twin-twin transfusion was unequal venous sharing without vascular anastomoses or patterns of vascular anastomoses typical for twin-twin transfusion. Also, the vascular pattern most commonly causing the highest perinatal mortality rate (No. 12) was the result of unequal venous sharing, arterio-venous vascular anastomoses and absence of superficial vascular anastomoses. Unequal venous sharing may be the substrate for arterio-venous vascular anastomoses if the arterial trees are of roughly equal size (Fig. 1).

Most monochorionic placentas had quite simple patterns of vascular anastomoses, and there were seldom multiple sites of arterio-venous vascular anastomoses in the cases with high mortality secondary to twin-twin transfusion. Since arterio-venous vascular anastomoses probably reflect differences in the sizes of venous "fields," they were most commonly found quite close to the insertion of the cord of the larger twin. In the context of twin-twin transfusion, this was the cord of the recipient twin, and the site of vascular anastomoses should be readily visible by fetoscopy because of hydramnios of the recipient.

The worst clinical outcomes (high rates of perinatal mortality, hydramnios, and growth discordance, and early gestational age at delivery) were found in twins lacking superficial vascular anastomoses, having unequal venous sharing, and with sites of arterio-venous vascular anastomoses. The presence of superficial vascular anastomoses appears to protect against the effects of arterio-venous vascular anastomoses, probably by allowing blood to return from the recipient to the donor. In the absence of superficial vascular anastomoses, uncompensated transfusion via arterio-venous vascular anastomoses results in bad outcomes. Similar results have been reported by Bajoria et al. [1995].

Patterns of vascular anastomoses in some placentas suggested that indiscriminate ablation of chorionic fetal vessels [De Lia et al., 1993] would result in poor venous return. However, methods for accurate prenatal mapping of arterio-venous vascular anastomoses zones are required before selective ablation can be applied.

In this series, 3 cases were managed by serial amniocentesis following the diagnosis of acute prenatal twin-twin transfusion in the second trimester. Most perinatal deaths were caused by severe prenatal twin-twin transfusion, and this was true of all cases in vascular anastomoses groups.

There is probably an excess of dichorionic twins among surviving monozygotic twin pairs who are used in twin studies of genetic and environmental causes of

TABLE III. Percentage of Dichorionic and Monochorionic Twins With Mild, Moderate, and Severe Growth Discordance*

	Growth discordance		
Chorionicity	Mild	Moderate	Severe
Dichorionic	53	26	21
Monochorionic	52	24	24

*Mild growth discordance: <9.99%. Moderate growth discordance: 10–19.9%. Severe growth discordance: >20%.

discordance. This is because of the high rate of perinatal deaths in monochorionic twin pairs. Such studies can be further refined with regard to prenatal and postnatal environmental influences if placental anatomy and vascular status are defined accurately at birth. Issues such as potential for growth catch-up in weight-discordant pairs can only be analyzed when placental status is known. Likewise, discordance for genetic disease and congenital anomalies can also be studied according to placental anatomy; for instance, some types of congenital heart disease in monochorionic twins may be "flow" lesions, resulting from disturbed early hemodynamics in twin pairs with placental vascular anastomoses.

Accurate placental vascular studies will add to the understanding of biological events in the large subgroup of monozygotic twin pairs who share monochorionic placentas.

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